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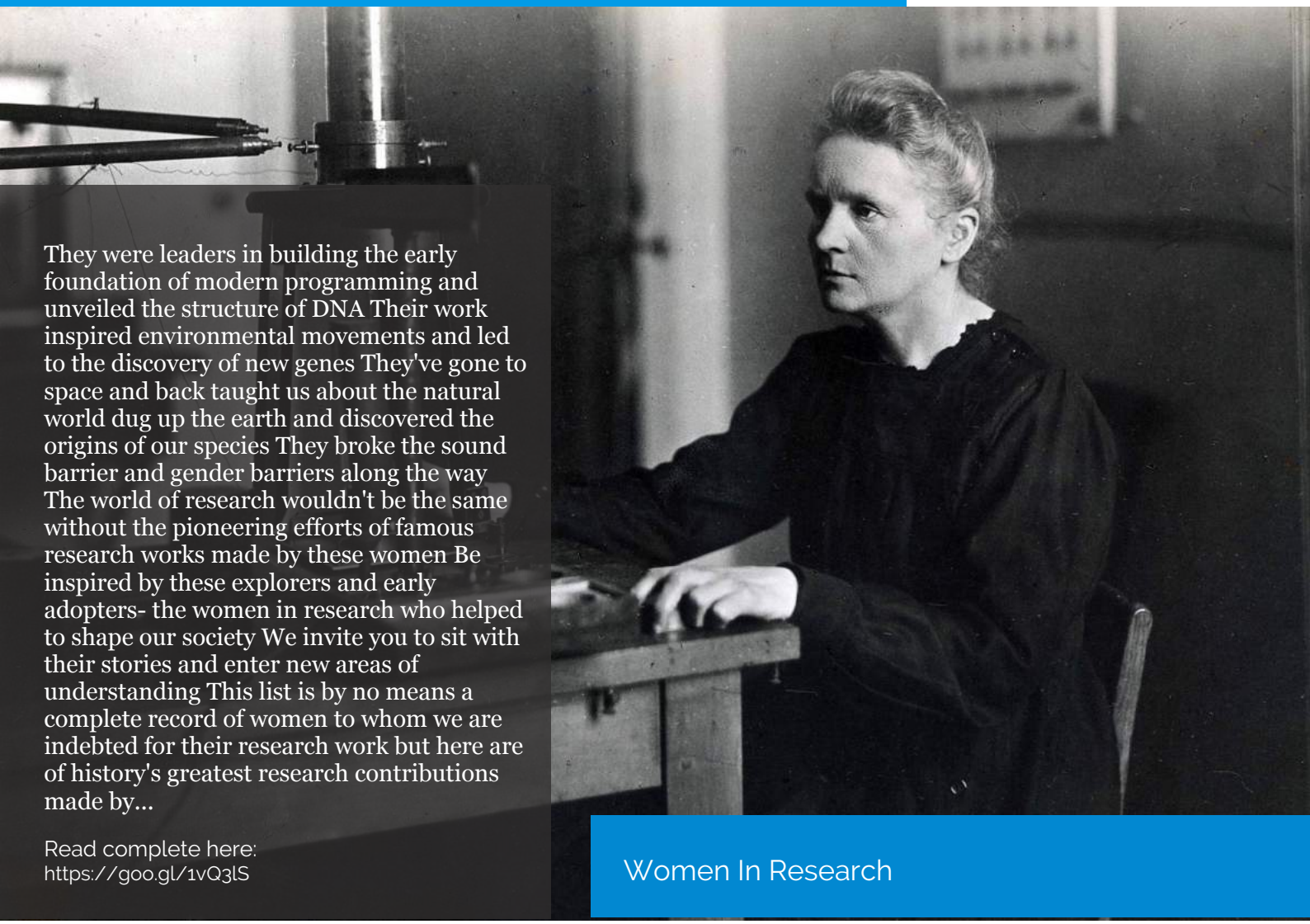

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The Influence of Sleep Quality on Chronic Pain

MSc. Regiane D. Sperandio, Gabriela Cristina de Oliveira, Matheus Casatti Silva, Dr. Renata Pletsch Assunção & Marcos Antonio Russi

Centre Padre Anchieta

ABSTRACT

Sleep is an essential physiological process that performs the maintenance of several mechanisms inherent to human homeostasis, being considered a healthy sleep, one that has quality and quantity determined to maintain a state of wakefulness during the day. According to the World Health Organization, 30% of the world population has chronic pain. Thus, the objective of this study was to verify the relationship between quality of sleep and chronic pain. This is therefore a field research, carried out via an online form, on pain characteristics and quality of sleep in individuals with chronic pain. The results achieved showed 42 valid answers, with individuals with a mean age of 34.25 (±11.30) years. The average intensity of pain was 4.70 (±2.09), and the quality of sleep was classified as good in 52.28% of the volunteers, although the majority of them slept less than 7 hours per night. Statistically the worse the quality of sleep, the greater the intensity of pain p=0.01, the worse the quality of sleep, the greater the feeling of not having rested, in which p= 0.03 and the worse the quality of sleep, the greater the sleepiness during the day with p= 0.007. We conclude that the greater the intensity of pain, the worse the quality of sleep of the individuals.

Keywords: sleep, circadian cycle, chronic pain.

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The Influence of Sleep Quality on Chronic Pain

MSc. Regiane D. Sperandio[α], Gabriela Cristina de Oliveira[σ], Matheus Casatti Silva[ρ], Dr. Renata Pletsch Assunção [Ↄ] & Marcos Antonio Russi[¥]

ABSTRACT

Sleep is an essential physiological process that performs the maintenance of several mechanisms inherent to human homeostasis, being considered a healthy sleep, one that has quality and quantity determined to maintain a state of wakefulness during the day. According to the World Health Organization, 30% of the world population has chronic pain. Thus, the objective of this study was to verify the relationship between quality of sleep and chronic pain. This is therefore a field research, carried out via an online form, on pain characteristics and quality of sleep in individuals with chronic pain. The results achieved showed 42 valid answers, with individuals with a mean age of 34.25 (±11.30) years. The average intensity of pain was 4.70 (±2.09), and the quality of sleep was classified as good in 52.28% of the volunteers, although the majority of them slept less than 7 hours per night. Statistically the worse the quality of sleep, the greater the intensity of pain p=0.01, the worse the quality of sleep, the greater the feeling of not having rested, in which p= 0.03 and the worse the quality of sleep, the greater the sleepiness during the day with p= 0.007. We conclude that the greater the intensity of pain, the worse the quality of sleep of the individuals.

Keywords: sleep, circadian cycle, chronic pain.

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I. INTRODUCTION

Sleep is an essential physiological process that performs the maintenance of several mechanisms inherent to human homeostasis, playing an active role in both cognition and health [1,2].

Sleep is typified in humans by 5 stages that are differentiated by the presence or absence of rapid eye movements (rapid eye movement: REM; no rapid eye movement: N-REM), in addition to various physiological variables, such as the cardiorespiratory pattern and muscle tone.

Reactivity to auditory, visual, tactile and painful stimuli is reduced or abolished in relation to vigil, particularly in deep sleep phases. A predictable sleep cycle is about 90 minutes, which traces the variation between the 4 stages from N-REM sleep to REM sleep [3].

The ideal average sleep time is 7 to 8 hours per night, however, the structure of sleep varies between individuals and their age therefore, a healthy sleep is one that has quality and quantity determined to maintain a state of wakefulness during the day [4].

The capability of the individual to adjust his/her sleep and wakefulness cycle is oriented by several external elements such as luminosity, temperature, sounds, as well as by the neurochemical bio-rhythm that comes with the circadian variations, with specific changes in body temperature and in the secretion of several hormones and neurotransmitters, related to different stages of sleep and wakefulness [3].

The supraoptic nucleus receives light impulses from the optic nerve stimulating the pineal gland to secrete melatonin, an essential neuro-hormone in the chronobiology of the sleep-wake cycle, having its peak in the first hours of the night and hence considered as one of the "gates" for entering sleep, thus, if the individual forces the

state of wakefulness fighting against sleep he/she loses the propitious moment to enter the state of sleep [3].

A range of evidences suggests that sleep, or the lack of it, may interfere with certain brain functions such as learning, memory and the regulation of endocrine and autonomic secretion According to the World Health Organisation (WHO), four out of ten people do not get good quality sleep, and sensitivity to pain can be modulated by the quality and quantity of sleeping hours [5,6].

According to IASP [7] (International Association for the Study of Pain) pain is defined as: "an unpleasant sensory and emotional experience associated, or similar to that associated, with a real or potential tissue injury", being also considered a subjective experience, influenced in various degrees by biological, psychological and social factors. The IASP recommends chronic pain as that one lasting more than six months, of continuous or recurrent condition (three episodes in three months).

Due to its long duration, chronic pain becomes no longer a warning sign, losing the ability to maintain homeostasis, leading to suffering and functional impairment, which progressively incapacitates the individual generating socioeconomic costs. More than one third of the Brazilian population deems that chronic pain compromises the usual activities and more than three quarters consider that chronic pain is limiting for recreational activities, social and family relationships [8].

The WHO estimates that an average of 30% of the global population suffers with chronic pain. In Brazil, this is equivalent to 60 million Brazilians.

Around 50% of those affected by the problem face routine impairment, such as absence and inability to work or even to perform the simplest tasks, estimates the Brazilian Society for the Study of Pain (SBED). Not surprisingly, 75% to 80% of medical attention in public services are motivated by complaints of pain, according to international epidemiological data, informs the Ministry of Health. [9]

The biopsychosocial approach claims that the experience of pain is determined by the interaction between biological factors including nerve pathways as well as biochemical processes, psychological factors covering emotions, thoughts, beliefs, expectations and attributions, and finally, social factors ranging from interpersonal interactions and sociocultural expectations [10].

Therefore, the aims of this study were to investigate whether there is a relationship between the quality of sleep and chronic pain, specifically to identify factors that may commonly impair sleep and pain concomitantly.

II. METHODS

This research is a field research approved by the Research Ethics Committee by the number CAAE: 58271822.0.0000.5386, in which a survey of data was carried out through an adapted form on pain characteristics and quality of sleep, which was based on the Pittsburgh form regarding sleep questions. The form was applied via Google Forms https://docs.google.com/forms/d/e/1FAIpQLSc8wwFfhe9yPLX07KipdbV371_W6Vz88IrsMuWhea8UukXnCg/view form), together with the Informed Consent Form (ICF), through social networks (Instagram, Facebook and WhatsApp).

The inclusion criteria included individuals over legal age suffering from chronic pain; and the exclusion criteria involved the non-agreement with the ICF, incomplete or improper completion of the form and individuals taking sleeping medication. There was no limit number of participants or geographical area delimitation.

Data collection was performed between June and August 2022 and subsequently data analysis was performed using Microsoft Windows 10 Excel spreadsheet and SPSS 22 software with ANOVA method considering significant results with $p \leq 0.05$.

III. RESULTS

General data

The research resulted in 101 responses given to the form, however, 59 participants were excluded, 07 of these did not present pain, 34 did not

answer any question related to sleep and 18 in which the pain does not fit chronic pain, which would compromise the objectives of this study.

Thus, 42 participants composed the present results, being 27 women (64.29%) and 15 men (35.71%).

The mean age of the participants was 34.25 years (±11.30). The high standard deviation is explained by the great discrepancy of age, in which the study counted on volunteers from 19 to 68 years old.

The mean age of women was 34.25 years (±11.30) and men 34.77 years (±11.30).

Physical activity was practiced by 57.14% of the volunteers (n=24), 41.66% of whom were female (n=10) and 58.33% male (n=14), and 42.86% (n=18) did not practice any type of physical activity, of whom 94.44% (n=17) were female and 5.55% (n=1) male.

Among the volunteers who practiced physical activity, three groups were defined, where group "A" defined muscle strengthening, representing 37.5% of participants (n=9), group "B" for those who practiced only aerobic activity, represented by 16.66% (n=4) of volunteers and group "C" for individuals who practiced both modalities of group A and B, consisting in this group 45.83% (n=11).

In terms of frequency of physical activity, it was diverse, from 2 to 6 times a week, with the following results: 2x=12.5% (n=3), 3x=29.16% (n=7), 4x =12.5%(n=3), 5x= 33.33% (n=8) and 6x = 12.5% (n=3).

The preferred times for training were divided into morning with 29.16% (n_=7), afternoon with 16.66% (n_=4), night with 45.83% (n_=11), and 8.33% (n_=2) of the volunteers trains at various times according to their availability.

It is noteworthy that none of the volunteers worked at night and slept during the day.

Pain Data

Regarding the characteristics of pain, the classification from 0 to 10 was adopted as a method to assess the intensity, and it was found that the mean pain level of the participants was 4.70 (±2.09). The distribution in the respective levels of pain can be observed in table 1 below.

Table 1: Pain intensity of the participants

Level of Pain 0-10	Number of participants	% Representation
02	06	14,29%
03	08	19,05%
04	05	11,90%
05	08	19,05%
06	03	7,14%
07	06	14,29%
08	04	9,52%
09	01	2,38%
10	01	2,38%

Caption: Left column represents the number of pain reference according to the numeric pain scale (0 to 10), the middle column represents the number of participants corresponding to the intensity of pain classification, and the right column represents the percentage of participants in each level of pain intensity. Source: The author herself.

By using the classification of pain as weak (levels 1 to 3), moderate (levels 4 to 6), strong (levels 7 to 9) and unbearable (level 10), the following results in the level of pain of the volunteers were obtained: weak 33.33% (n=14), moderate 38.09% (n=16), strong 26.19% (n=11) and unbearable 2.38% (n=1).

The interference of this pain in sleep is described by 26.19% (n=11) who reported waking up in the middle of the night due to pain, however, the great majority of volunteers 73.81% (n=31) do not wake up during the night due to pain.

Sleeping Data

A survey of the amount of hours of sleep was carried out by the volunteers, the results are presented in table 2 below:

Table 2: Amount of hours slept per night by the volunteers

Sleeping hours	Quantity of answers	% Representation
4h	1	2,38%
4h30	1	2,38%
5h	2	4,76%
5h30	5	11,90%
6h	12	28,57%
6h30	3	7,14%
7h	9	21,43%
7h30	2	4,76%
8h	4	9,52%
+ de 8h	2	4,76%
Not specified (insomnia)	1	2,38%

Caption: Left column indicates the amount of hours of sleep per night; middle column the amount of volunteers who fit into a certain sleep time and in the right column the percentage of participants for each sleep period. Source: The author herself.

It is highlighted that 59.52% (n=25) of the participants slept less than 7h per night, 26.19% (n=11) slept between 7 and 7h30 and only 14.28% (n=6) slept 8h or more as recommended by the WHO.

When analysing the quality of sleep from the point of view of the volunteers, the following results were obtained: very good sleep 7.14% (n=3), good 52.38% (n=22), bad 33.33% (n=14) and very bad 7.14% (n=3). However, despite the positive rate in reporting sleep quality as good, the feeling of NOT having rested during sleep was expressed by 76.19% (n=32) of the participants with only 23.80% (n=10) of those with the perception of sleep having been restorative.

Another evaluated element was sleepiness on the part of the participants during their daily activities, in which 76.19% (n=32) reported feeling sleepy during their daily activities, while only 23.80% (n=10) reported not feeling sleepy during the day. Only one of the volunteers (2.38%) did not feel sleepy during the day and did not use stimulants for the Central Nervous System.

Regarding the use of these substances, 52.38% (n=22) make use of some type, such as chocolate, tea, ginseng, cinnamon, energy drink and coffee, the latter being used by 90.90% (n=20) of those who use stimulants, and 47.61% (n=20) do not use this class of substances.

Further analysis was carried out on the perception of the volunteer on the quality of sleep and the worsening of pain, in which 64.29% (n=27) stated that whenever they slept badly the next day they reported worsening of the pain, or still, that when the intensity of pain was greater during the day, the quality of sleep was worse, and 35.71% (n=15) of the participants could not make this correlation.

IV. RELATION BETWEEN DATA

In the analysis of the pain of the individuals associated with the quality of sleep, it can be observed in table 3 below, that most of the volunteers refer to good quality sleep, and these fall within the intensity of weak to moderate pain, and as the intensity of pain increases to strong, most refer to poor quality sleep.

In the statistical analysis of these data, it was found that the worse the quality of sleep of the individual, the greater the intensity of pain, with a high degree of significance where p=0.01.

Table 3: Relation between pain level and quality of sleep

Level of pain	Quantity of individuals	Very good sleep	Good Sleep	Bad sleep	Very bad sleep
Weak	14 (33,33%)	3 (21,43%)	9 (64,29%)	2 (14,29%)	----------
Moderate	16 (38,09%)	----------	9 (56,25%)	5 (31,25%)	2 (12,5%)
Strong	11 (27,19%)	----------	3 (27,27%)	7 (63,64%)	1 (9,09%)
Very strong	1 (2,38%)	----------	1 (2,38%)	----------	

Caption: Column on the left refers to the intensity of pain classified as weak, moderate, strong and very strong, followed by the number of volunteers who referred pain in these intensities and subsequently the amount of participants who fit each type of sleep, on a scale from very good to very bad. Source: the author herself.

Table 4 below shows the relationship between sleep quality and the feeling of not having rested after the rest period, and the presence of sleepiness during the day and as a result, it can be seen that the worse the quality of sleep, the greater the feeling of not having rested, where p= 0.03 and the worse the quality of sleep, the greater the sleepiness during the day with p= 0.007.

Table 4: Sleep quality and feeling NOT rested & sleepiness during the day

Sleep Quality	Feeling not rested	Sleepiness during the day
Very good 7,14% (n=3)	Yes = 66,67% (n=1) No = 33,33% (n=2)	Yes = 66,67% (n=1) No = 33,33% (n=2)
Good 52,38% (n=22)	Yes = 63,64% (n=14) No = 36,36% (n=8)	Yes = 72,72% (n=16) No = 63,64% (n=6)
Bad 33,33% (n=14)	Yes =100 % (n=14) No = 0% (n=0)	Yes = 85,71% (n=12) No = 14,29% (n=2)
Very bad 7,14% (n=3)	Yes 100%= (n=3) No = 0% (n=0)	Yes = 100% (n=3) No= 0% (n=3)

Caption: The left column shows the reference of the volunteer regarding his/her quality of sleep, in the middle column the number of volunteers who had the sensation of not having rested during the night and its relation with the level of pain; the right column shows the number of individuals who reported sleepiness during the day. Source: author herself.

Another relation analysed was the practice of physical activity, the schedule of practice and pain intensity. Table 5 below shows that the majority of individuals with intense pain do not practice physical activity. The relationship between physical activity and pain presents a statistical analysis with p≤0.001, proving that sedentary individuals present greater intensities of pain.

Table 5: Pain level and physical activity practice

Pain level	Practice of Physical Activities	Schedule of physical activity
Weak (n=14)	Yes = 78,57% (n=11) No = 21,43% (n=3)	Morning = 36,36% (n=4) Afternoon = 18,18% (n=2) Evening = 45,45% (n=5)
Moderate (n=16)	Yes = 62,5% (n=10) No = 37,5% (n=6)	Morning =20% (n=2) Afternoon = 30% (n=3) Evening = 50% (n=5)

Strong (n=11)	Yes= 27,27% (n=3) No= 72,73% (n=8)	Morning =33,33% (n=1) Afternoon = 33,33% (n=1) Evening= 33,33% (n=1)

Caption: Left column shows the level of pain (weak, moderate or strong), middle column shows the number of individuals who do or do not practice physical activity, and in the right column the time of day that these individuals practice physical activity. Source: The author herself

V. DISCUSSION

It is recommended a total sleep time greater than 7 hours for the population in general, since sleep is responsible for regulating the body's homeostasis, being essential for the cognitive and physiological recovery of individuals [11,12]. In this study, it was observed that 59.52% (n=25) of the volunteers slept less than 7 hours per night, not following the recommended amount of sleeping hours.

Researchers suggest that some lymphokines do promote NREM sleep, such as the tumour necrosis factor alpha (TNF-α) and interleukin-1 (IL-1), which means that these substances can regulate physiological sleep, as well as other molecules from the immune system. The main symptom in individuals with sleeping disorders is excessive daytime sleepiness, and these normally present with elevated interleukin-6 (IL-6) in the blood [13-15]. In this scenario, it was found that 76.19% (n=32) of the volunteers in this study reported feeling sleepy during the day. It is worth mentioning that no blood analysis was performed on the volunteers.

While healthy sleep facilitates immune functions, impaired quality or quantity of sleep can result in a low-grade inflammatory response, the response as a consequence of sleep deprivation includes increased levels of nitric oxide (NO), prostaglandin E2(PGE2) and IL-6, and possibly mediated by glia cells [16].

Sleep deprivation imparts a low-grade inflammatory response, leading to increased pain sensitivity, as observed in individuals with chronic pain [16], in which the subjects of this study fit.

Nowadays, it is known that the treatment of chronic pain is complex and, in order to be effective, a multidisciplinary approach is required, with physical exercises being a key part of the treatment, since physical activity, besides being indicated as a non-pharmacological intervention with positive results for the treatment of chronic pain, is an accessible therapy from the economic point of view [17-19].

It is observed in this study that 51.4% (n=24) of the volunteers practices some type of physical activity, and even so, they are affected by chronic pain. Although the clinical benefits of exercise in reducing the intensity of chronic pain are highlighted, the physiological effects involved are still unclear; sometimes the analgesic effect is contradictory [20]. One of the most described hypotheses to explain this increase in pain threshold - comparing athletes or active and sedentary people - is the influence of the practice of activity and/or physical exercise on endogenous mechanisms, which leads to the opioids release [21,22].

Although the majority of volunteers in this research practiced physical activity, pain was present in all volunteers, it was also observed that 33.33% (n=14) of the volunteers had pain of low intensity, in which 78.57% (n=11) did some activity, 38.09% (n=16) presented pain of moderate intensity, of these, 62.50% (n=10) practiced exercises, and 27.19% (n=11) reported pain of strong intensity, where only 27.27% (n=3) had physical activity in their routine of life.

Researches elucidate the findings of this study, since they concluded in their studies that physical exercises can be beneficial in reducing the intensity of chronic pain and in general aspects of quality and physical and mental health [23-25].

Souza [26] adds to the authors above that exercise does not need to be of high intensity to have an effect on pain, concluding his research by affirming that moderate intensity aerobic exercise for more than 10 minutes is able to activate endogenous mechanisms of pain control in healthy individuals.

In a study conducted among elite athletes describes that behavioural factors related to the athlete's routine seem to be more important for injury and pain, singling out sleep, which includes the amount of hours slept and the quality of sleep [27]. Other studies [28,29] reported that sleep deprivation leads to a reduction in the production of growth hormones (GH) and testosterone, as well as an increase in cortisol, thus directly affecting the organism's homeostasis as defined by Hirshkowitz 12, a factor to be considered in the volunteers of this study.

The time of doing physical activity in this study, according to the participants, was predominantly during the evening, with 45.83% (n=11) training at this time of day. Stutz and collaborators [30] stated in their study that the exercises practiced at evening do not interfere negatively in sleep, as long as the time of exercise is up to one hour before bedtime and high intensity. Wendt et al [31] showed divergent results, in which the practice of evening physical activity resulted in a negative effect on sleep, not depending on the intensity, but in relation to daytime physical activity, which showed positive results on sleep·

Kraemer [32] reports in a study that although the neuroendocrine adaptations seem minimal, the hormonal response depends on the intensity, volume, involvement of muscle mass, rest intervals and frequency, where high volume and moderate to high intensity exercises tend to produce higher elevations of anabolic hormones such as GH and testosterone, but also of cortisol, which is a catabolic hormone involved in the sleep process. Other researchers [33-36] corroborate with Kraemer [32], that the relation of physical activity and its duration/intensity with the level of cortisol, in which, when it is performed with a high level of effort and/or stress, either by intensity or duration, there is an increase in the level of cortisol. Upon physical exercise there is secretion by the hypothalamus of the hormone that releases corticotrophin, activating the pituitary gland, where it stimulates the release of adrenocorticotropin, which stimulates the release of cortisol by the adrenal cortex. In the present study, the volume/intensity of the physical activity performed by the volunteers was not evaluated, but its close relationship with the results presented here is assumed.

The NREM sleep is regarded as the restorative sleep phase; authors have reported that the increase in cortisol at night reduces the REM sleep phase and increases the NREM phase, which is explained by a biphasic effect of cortisol, in which up to a certain level, it favours the REM phase, but when it is too high, it inhibits it [37]. In the present study, it was verified that 76.19% (n=32) of the volunteers reported waking up feeling tired, even though the majority, 52.38% (n=22) reported a good quality of sleep, which makes us wonder about the connection of cortisol levels among these volunteers.

Another factor to be considered is that 52.38% (n=22) of the participants in this study use some kind of stimulant substance during the day, especially coffee, used by 90.90% (n=20 of the 22 who take stimulants). Caffeine activates the stress axis, raising glucocorticoids and catecholamines[38].

The effect of caffeine on glucocorticoid regulation has, therefore, the potential to alter circadian rhythms and interact with stress[39], which can be a factor related to changes in the quality of sleep, as well as associated with chronic pain in the participants of this study, since 64.29% (n=27) of them described that after a bad night's sleep, their pain worsened.

Hence, the relationship between sleep disturbance and chronic pain would probably be best characterised as a reciprocal vicious circle, with pain contributing to sleep disturbance and also contributing to increased pain sensitivity[40].

Araújo and collaborators[6] corroborate with Smith[40] stating that reduced sleep time increases the response to pain and chronic pain conditions are capable of altering the sleep pattern.

VI. CONCLUSION

Sleep has an important function in the balance of the organism, and a non-restorative sleep or sleep of less than seven hours can cause an inflammatory response, increasing sensitivity to pain. Most participants in this study slept less than seven hours, not following the WHO recommendations, and although most of the

volunteers classified their sleep as of good quality, it was found that 76.19% of the individuals in this study reported waking up with the sensation of not having rested. Tiredness upon waking up, as well as sleepiness during the day, was more frequent in the volunteers with greater intensity of pain, being an inconsistency when they report having good quality sleep.

On the other hand, the practice of physical activity is being shown as one of the main and most important forms of treatment in the control of chronic pain, since it can trigger the release of endogenous opioids that act in the pain sensitivity control. Most participants practiced physical activity and reported weaker pains when compared to sedentary individuals, whose pain had a greater intensity, indicating that exercise is a beneficial factor, however, the intensity of physical activity may be related to the inflammatory index of the body and the release of substances such as cortisol and IL-6 in the organism. Added to other factors such as coffee, which is frequent in the routine of the volunteers of this study, the quantity of circulating inflammatory hormones and cytokines in the organism may be directly linked to cases of chronic pain, as well as, associated to poor quality of sleep, with the conclusion being that the greater the intensity of pain, the worse the quality of sleep. Nevertheless, new studies are necessary, in which it is possible to measure the intensity of exercises, the quantity of circulating hormones and cytokines for more complete results in the population that suffers with chronic pain.

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Factors of Non-Use of Modern Contraception from 2006 to 2017 among Married or Cohabiting Women in Benin

Guy Armand Onambélé & Vignon Constant Tchoukou

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Objective: The aim of this study is to analyze the overall trend in factors of the non-use of modern contraceptive methods among married or cohabiting women from 2006 to 2017.

Data and methods: The data analyzed come from the Benin Demographic and Health Surveys (EDSB) conducted in 2006 and 2017-2018. The description of contraceptive variation was done using bivariate descriptive methods, the identification of resistance factors to contraceptive use from a binary logistic regression model and the analysis of observed changes in contraceptive practice from 2006 to 2017 by the Oaxaca-Blinder multivariate decomposition method.

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Results: Fear of side effects and opposition from women or partners were the main reasons given by women in a union in 2006 (21.0%; 11.4%) and 2017-2018 (18.4%; 35.5%) for refusing to use modern contraceptives. At the bivariate level, except for the variable information received on family planning in 2017 and the number of child deaths, a significant association at the 1% level was established between the non-use of modern methods and the independent variables. However, a decrease in proportion was recorded in the different subgroups of variables and especially in contraceptive decision-making.

With a difference of 51 points, 70.8% of women reported not deciding to use contraceptives within the couple in 2006 versus 19.5% in 2017.

The Oaxaca-Blinder multivariate decomposition revealed that 87.5% of the observed changes in contraceptive use were due to differences in coefficients and 12.4% to differences in characteristics. Family planning information, religion, department of residence, household standard of living, number of deceased children, contraceptive decision, and husband's desire to have children were significantly associated with the non-use of modern contraceptives between 2006 and 2017.

Recommendations: Family planning programs and policies should be strengthened in all departments by involving spouses and partners more. Lifestyle improvement measures should be encouraged to ensure equitable access to contraceptives.

Keyword: Benin, family planning, contraception, reproductive health, women.

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I. INTRODUCTION

After the 1994 Cairo conference, international support for family planning impacted millions of people through its role in reducing poverty, improving health and human development. Benin has not remained on the sidelines of these changes and in its commitment to controlling its population growth. It has undertaken a series of reforms to its health system to promote reproductive health through the Ministry of Health by offering family planning services in all

health facilities (Ministry of Health, 2012). These actions are reinforced by the remarkable support and intervention of several Technical and Financial Partners (TFPs) and Civil Society Organisations (CSOs). In 2020, the additional number of Beninese women using modern contraception was estimated at 204,000, the modern contraceptive prevalence rate at 13.0%, and the unmet need for modern contraception at 35.3% (Scoggins S and al, 2020).

In addition, it is estimated that 131,000 unintended pregnancies, 46,000 unsafe abortions and 340 maternal deaths will be averted by modern contraception in 2019. Therefore, women's use of contraceptive methods has economic, health, and social benefits for the community. Despite these efforts, the contraceptive security index in Benin remains relatively low, calling for additional initiatives to achieve the goals related to new aspirations in reproductive health and contraceptive practice (USAID, 2012). Today, opposition to the use of modern contraceptive methods, particularly among women in union, is perceptible in Beninese society, with disparities between regions. Hence the importance of understanding the obstacles to the utilization of modern contraceptives within couples. This study aims to analyze the evolution of the determinant factors of the non-use of modern contraception among women in a union in Benin between 2006 and 2017.

1.1 Literature Review

Several research studies have explored the different facets of family planning (FP), of which contraceptive practice is one of the topics of interest in demographic research (Ngo Mayack and al., 2019). Women's FP behaviors are analyzed under the prism of service supply and demand. According to Morhason-Bello IO and al (2022), the low level of family planning uptake in Nigeria is due to demand and supply side factors.

1.1.1 Service delivery approach

According to this approach, the decision to use contraception depends on the availability and accessibility of services, which consider several dimensions. Availability refers to the existence of suitable FP service centers and, above all, the availability to the population of a variety of modern contraceptive methods capable of stimulating the use of family planning services.

The accessibility of services, it refers to geographical, economic, administrative, cognitive, and psychosocial accessibility (Bertrand JT et al, 1995).

Geographical accessibility indicates the physical location of services in relation to the place of residence of households and the obstacles encountered by the latter to access the products made available. Indeed, the further away the health facility offering FP services is, the fewer women use it (Moussa Z, 2011). Accessibility to family planning services improves women's knowledge and practice of contraception.

Economic accessibility relates to the affordability of the direct and indirect costs of contraception, which are the unit selling prices of contraceptive products, the expenses related to consultation and travel as well as the waiting time in health centers influence the use of FP services (Rwenge M., and al, 2019) and therefore the choice of contraceptive method. Indeed, the high cost of modern contraception and the quality of services offered are constraints for economically disadvantaged women to use traditional methods more than modern ones. Administrative accessibility refers to the institutional and legal framework that can influence contraceptive practices. The policy context is the normative framework for FP intervention, where laws and regulations, as well as strategies and programmes that govern contraceptive behavior, are defined. For example, some laws that require a woman to have her husband's permission to use contraception restrict women's access to family planning services (Lenan G., 2009). Cognitive accessibility provides information on individuals' knowledge of contraceptive methods and FP centers. A study conducted in the Mumbunda health zone in Lubumbashi, DRC, showed that women with a high level of knowledge about contraceptive methods were twice as likely to be users of contraceptive methods as those with a low level of knowledge (Charles M., and al, 2015).

Psychosocial accessibility addresses social factors that may prevent a woman from comfortably adopting better contraceptive practices. These include beliefs and stereotypes about contraception etc.

1.1.2 Demand Approach

This approach encompasses three dimensions that are decisive in the decision to use or not to use contraception. These are the economic, socio-cultural, and socio-demographic dimensi--ons.

1.1.2.1 Economic dimensions of demand

Low-income households are facing financial challenges in terms of the cost of counseling, contraceptive supplies and transportation which limit their access to family planning services. According to the results of the fifth Benin Demographic and Health Survey, the percentage of women in union with a high quintile of economic well-being who use modern contraception is double their counterparts with the lowest level of economic well-being (INSAE, 2017). Furthermore, occupation (type of economic activity) is also likely to influence contraceptive practices among women. In this context, Nounké K. (2011) notes that women in the modern sector, due to specific difficulties linked to their activity, including those of reconciling the function of mother and professional, tend to control their birth by resorting to the use of contraceptives.

1.1.2.2 Socio-cultural dimensions of demand

Cultural factors are equally important in understanding couples' choice of family planning and contraception (Mbarambara P. and al, 2016). Several authors have highlighted the central role of elements of tradition in explaining reproductive behavior in families. According to Noumbissi A. and al (2000), the low prevalence of modern contraception is due to the pro-natalist mentality maintained by the norms and values of the culture that values high fertility. Indeed, the perception of children in traditional African societies reflects a preference for high fertility among couples. This does not encourage a strong demand for contraceptive methods. In Africa, not only is the child considered a gift from God that perpetuates the family lineage, it is also a gain (or wealth) for the parents and therefore supposed to ensure their economic and social development (Kouadio A and al, 2015). These social representations of the child justify couples' reluctance to regulate births through modern contraception.

Furthermore, the social environment characterized by ethnicity, place of residence during childhood and religion influences women's contraceptive practices as well as the environment in which fertility is achieved and whether or not they live with their spouse (Mayack J., and al 2017).

1.1.2.3 Socio-demographic dimensions of demand

Age appears to be one of the reasons for contraceptive failure, the immediate conse-quences of unwanted pregnancies and sexually transmitted infections and diseases (STIs). In Brazil, the work of Da Costa Leite, I. and al (2007) has shown that the risk of contraceptive failure decreases at older ages in women and this may be due to the decline in their fertility. The relationship between women's marital status and contraceptive use is established in the African context. Thus, sexually active women who are single or in a broken union (divorced, widowed) are more predisposed to the use of modern contraceptive methods than those in a conjugal union for economic and social reasons at times (Fassassi R., 2006). Women's fertility plans, which are reflected in their desire or refusal to have additional children, may lead them to adopt specific contraceptive behaviors. In this case, contraception represents a strategy for stopping births. The risk of not using contraception increases with the occurrence of childbirth and the desire of women to have both sexes in their offspring. The results of the study by Vignikin K. (2004) go to the same direction. Among other things, the gender relationship, which is illustrated by the man's involvement in favor of contraception, his opinion and the dialogue within the couple on family planning issues, was recognised as influencing the woman's contraceptive behavior. Regarding spousal exchanges, the study conducted by Charles M. and al (2015), showed that women who frequently

discussed with their partners were 6 times more likely to use modern contraceptives than those who never discussed. On the other hand, the spouse's profile, such as education level and occupation, was also admitted as a factor that may affect a woman's decision whether or not to use contraception for the total satisfaction of her FP needs.

II. METHODS

2.1 Data sources

The data for this survey comes from the Benin Demographic and Health Surveys (BDHS) conducted in 2006 and 2017-2018. Their sampling is based on a two-stage stratified cluster survey. In the first stage, clusters were chosen proportionally to their size from the list of DZs. In the second stage, households in which women were surveyed were selected randomly with equal probability from each cluster. This is a quantitative study with an analytical focus.

Married or cohabiting women aged 15-49 are the study population. According to the two survey rounds, there is a nationally representative sample of 13403 and 11169 women in a union in 2006 and 2017-2018 respectively. This data source is appropriate due to the good quality of contraception data collected.

2.2 Variables

2.2.1. Dependent variable

Information on contraceptive means or methods was collected from women in both DHS (2006 and 2017-2018). The variable to be explained is the non- use of modern contraceptive methods.

The study focuses on women in unions consisting of women aged 15-49 who are married or cohabiting at the time of the survey. The dependent variable is dichotomous, taking the value of 1 if the woman is not currently using any modern contraceptive method and 0 if she is using a modern method of contraception.

2.2.2. Independent Variables

The explanatory variables of the study take into account the supply and demand dimensions. These include: information received by the respondent on FP from community health workers, exposure to the mass media, place of residence, department of residence, religious affiliation, the woman's level of education, age, number of living children (parity), number of deceased children, the woman's professional occupation, the household's standard of living, the contraceptive decision and the husband's desire to have children

2.3 Analysis

Analysis process followed three steps. First, we describe the variation in the non-use of modern contraception according to the different characteristics. We evaluate the association between the dependent variable and each of the independent variables using the chi-square test at the 5% threshold ($p<0.05$). In the second step, we looked for the determinants of the non-use of modern contraceptive methods between 2006 and 2017 using a binary logistic estimation. We then applied the Oaxaca-Blinder multivariate decomposition method to analyze the changes observed in the evolution of modern contraceptive practice over the last eleven (11) years.

2.3.1 Oaxaca-Blinder Multivariate Decomposition Method

The Oaxaca-Blinder decomposition was used to identify and quantify the variables that contributed most to the decline in the proportion of women not using modern contraception between 2006 and 2017. In addition, the Oaxaca-Blinder decomposition technique generally describes the average difference in the variable of interest between two groups. This difference is comprized in two effects or components. First, the characteristics (or endowment) effect explains the difference between groups by the different levels of the observed characteristics. Second, the coefficient effect, again defined by the unexplained component, is closely associated with differences in the coefficients attributable to unobservable variables.

In this study, we opted for the Oaxaca-Blinder decomposition based on logistic regression. The general expression of the non-linear

decomposition of which the Oaxaca-Blinder decomposition is a part is written as

$$\overline{Y^1} - \overline{Y^2} = \underbrace{\left[\frac{1}{N^1}\sum_{k=1}^{N^1} F\left(\beta^1 X_k^1\right) - \frac{1}{N^2}\sum_{k=1}^{N^2} F\left(\beta^1 X_k^2\right)\right]}_{\text{Explained share}} + \underbrace{\left[\frac{1}{N^2}\sum_{k=1}^{N^2} F\left(\beta^1 X_k^2\right) - \frac{1}{N^2}\sum_{k=1}^{N^2} F\left(\beta^2 X_k^2\right)\right]}_{\text{Unexplained share}}$$

$\overline{Y^1} - \overline{Y^2}$ Difference in the probability of the predicted mean of the dependent variable (in this case non-use of modern contraception) between the two groups with N^1 the number of individuals in group 1 (i.e. year 2006) and N^2that of group 2 (i.e. year 2017);

F: Cumulative distribution function ;
Xk: the matrix of k independent variables and β a vector of logistic regression coefficients.

III. RESULTS

3.1 Changes in non-use of modern contraception by characteristics

The proportion of married or cohabiting women who do not use modern contraceptive methods fell between 2006 and 2017 from 93.9% to 87.6% respectively, a decrease of 6.3%.

The proportion of women not exposed to the mass media who do not use modern contraception has decreased by 7.2 percentage points between 2006 and 2017. The same is true for women in union who have not received information on FP from community health workers (6.2%). Analysis by area of residence shows that the percentage gap of married or cohabiting women in rural areas not using modern contraceptive methods is decreasing (6.2%) compared to women in urban areas (1.1%). At the departmental level, Mono experienced the greatest decline in the number of women in union who do not use modern contraception, followed by Alibori and Zou, with a 13.7%, 9.5% and 9.3% difference, respectively. On the other hand, the proportion remained unchanged among women in Couffo, with a 0-point difference. Concerning religion, the drop in the proportion of women who do not use modern contraceptive methods is high among women who practice Christianity (6.7%) between 2006 and 2017. In the same period, there was a decrease of women not using modern contraception who had no education, a reduction of 6.4 percentage points. We also note that adolescents aged 15-19 years use modern contraception less, even if their proportion fell slightly from 2006 to 2017 (2.3%). On the other hand, contraceptive prevalence is increasing among women farmers (5.3%) and in other sectors (6.5%) as well as among women from poorer (7.0%) and middle-income households (6.9%). In the same way, we record a low prevalence of non-use of modern contraception from 2006 to 2017 among women in unions who have 4 or more children. This suggests that from 4 live births onwards, women seek to control or limit their reproduction. On the other hand, women who have never had a deceased child are less likely to use contraceptive methods, by 5.8 percentage points between 2006 and 2017. The proportion of women who decide to use contraception within their couples increased significantly between 2006 and 2017. The difference in contraceptive prevalence is estimated at 51.2% when the decision is made by the woman, 44.5% when the decision is made together, and 26.1% when the decision to use contraception is made by the man alone. Women whose spouses or partners want fewer children tend to use modern contraceptive methods more. The proportion of these non-users fell from 89.6% in 2006 to 82.5% in 2017.

Table 1: Percentage of married or cohabiting women aged 15-49 not using modern contraception by selected characteristics

Independent variables	EDSB 2006		EDSB 2017-2018		Difference
	%	N	%	N	
Exposure to mass media					
Yes	91,4	6296	85,6	4409	-5,8
No	96,5	6283	89,3	5373	-7,2
Pearson chi2	p=0,000		p=0,000		
Information on FP for community health workers					
No	93,9	4200	87,7	2912	-6,2
Yes	87,5	1244	86,4	1790	-1,1
Pearson chi2	p=0,000		p=0,153		
Place of residence					
Urban	91,0	4434	85,5	3787	-5,5
Rural	95,5	8144	89,0	5995	-6,5
Pearson chi2	p=0,000		p=0,000		
Department					
Alibori	96,0	1097	86,5	1340	-9,5
Atacora	94,9	819	90,0	803	-4,8
Atlantic	94,8	1462	86,3	1131	-8,6
Borgou	93,3	1190	88,0	1215	-5,4
Hills	89,7	873	81,9	604	-7,9
Couffo	95,5	1074	95,5	710	0,1
Donga	96,1	515	94,1	674	-2,0
Coastal	89,2	925	80,8	445	-8,4
Mono	95,7	776	82,0	421	-13,7
Ouémé	91,0	1684	84,8	835	-6,2
Tray	96,6	697	94,3	668	-2,3
Zou	96,0	1466	86,7	936	-9,3
Pearson chi2	p=0,000		p=0,000		
Religion					
Endogenous	96,7	2505	91,4	1038	-5,3
Muslim	94,6	2948	89,4	3279	-5,3
Christian	92,2	6409	85,6	4937	-6,7
Without religion	95,6	683	89,0	529	-6,6
Pearson chi2	p=0,000		p=0,000		
Woman's level of education					
No	95,6	9425	89,2	6612	-6,4
Primary	91,2	2175	85,2	1689	-6,0
Secondary and above	84,3	979	83,4	1481	-0,9
Pearson chi2	p=0,000		p=0,000		
Age group					
15-19 years	97,1	648	94,8	586	-2,3
20-29 years	94,9	5272	88,8	4107	-6,1
30-39 years	92,5%	4271	84,7%	3168	-7,9%
40-49 years	93,1%	2388	87,9	1922	-5,1
Pearson chi2	p=0,000		p=0,000		
Occupation Woman					
Inactive	94,8	1565	90,9	1585	-4,0
Administration	82,2	203	80,1	293	-2,1
Agriculture	96,2	4519	90,9	2255	-5,3
Other sector	92,4	6233	85,9	5650	-6,5
Pearson chi2	p=0,000		p=0,000		
Household standard of living					
poorer	97,6	2576	90,6	1962	-7,0

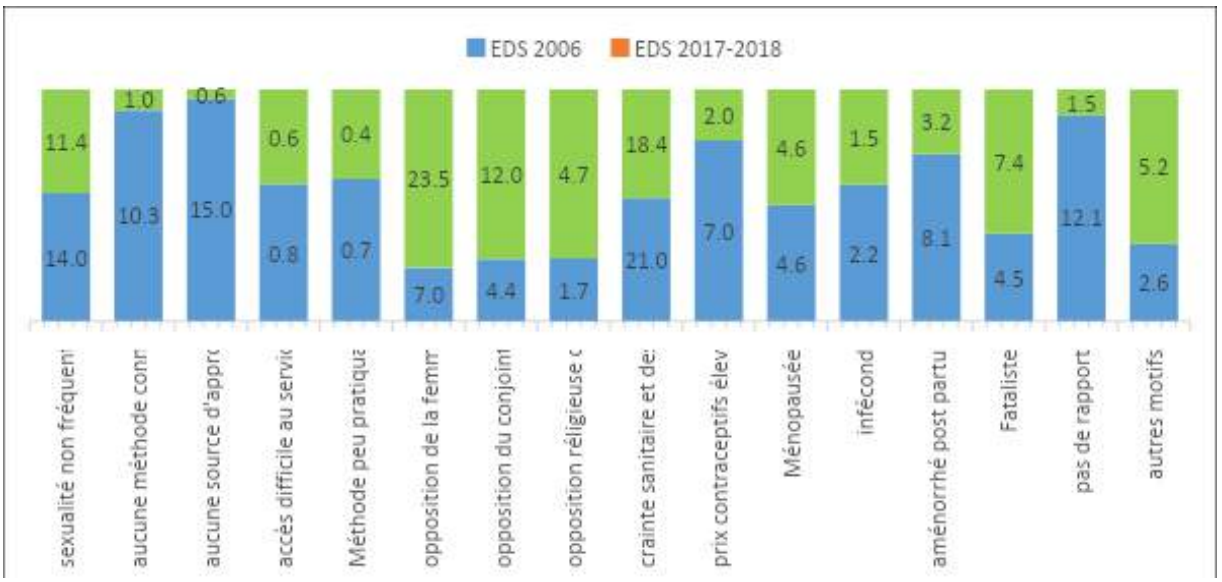
Independent variables	EDSB 2006		EDSB 2017-2018		Difference
	%	N	%	N	
Poor	96,3	2563	90,1	2000	-6,2
Medium	95,0	2595	88,1	1967	-6,9
Rich	93,3	2602	87,1	2030	-6,2
richer	86,8	2242	82,1	1823	-4,7
Pearson chi2	p=0,000		p=0,000		
Parity achieved					
0	98,6	716	98,7	607	0,1
1	95,0	1770	90,1	1491	-4,9
2	93,7	1976	89,4	1576	-4,2
3	93,7	1847	87,9	1507	-5,9
>=4	93,1	6734	84,9	4602	-8,2
Pearson chi2	p=0,000		p=0,000		
Number of children who died					
0	93,6	8067	87,8	7103	-5,8
1	93,8	2622	86,9	1716	-7,0
2	94,0	1123	87,8	631	-6,2
3	95,9	464	85,0	202	-10,9
4	96,9	186	90,7	82	-6,2
>=5	98,3	116	91,1	48	-7,2
Pearson chi2	p=0,041		p=0,517		
Contraceptive decision					
Woman	70,8	423	19,5	157	-51,2
Male	58,7	181	32,6	63	-26,1
Joint decision	61,7	801	17,2	126	-44,5
Pearson chi2	p=0,000		p=0,000		
Husband's desire for a child					
joint desire for the number of children	91,0	3675	84,2	2463	-6,9
the husband wants more children	95,2	3954	88,9	3807	-6,3
the husband wants fewer children	89,6	464	82,5	474	-7,1
Don't know	96,5	4446	90,3	3039	-6,2
Pearson chi2	p=0,000		p=0,000		

Source: EDSB data mining, 2006 and 2017-2018

3.2 Reasons for not using Modern Contraception among Women in Union between 2006 and 2017

Figure 1 shows that fear of health side effects is one of the main reasons cited by women who are not using modern contraceptive methods in 2006 and 2017, i.e. 21.0% and 18.4% respectively. In 2017, wifes (23.5%) and spouses (12.0%) did not use contraceptive methods. Moreover, while knowledge of no source of supply was the second most important reason given by women in 2006 (15%), it was relegated to last place among the causes for not using modern contraception, along with difficult access to FP services in 2017.

Similarly, infrequent sexuality (14.0% in 2006; 11.4% in 2017) and sexual inactivity (12.1%) in 2006 also played a considerable role in the non-use of modern contraceptive methods among women in a union during 2006 and 2017.



Source: EDSB data mining, 2006 and 2017-2018

Figure 1: Distribution of the proportion of women in union by reason for not using modern contraception

3.3 Explanatory factors for non-use of Modern Contraception among Women in Union between 2006 and 2017

According to the logistic estimation results presented in Table 1, information received on FP, religion, department of residence, household standard of living, number of deceased children, couple's decision to use contraceptives, and spouse's desire for additional children are the factors statistically associated with non-use of modern contraceptive methods among women in a union between 2006 and 2017.

On the one hand, in 2006 women who did not receive FP information from community health workers were twice as likely not to use modern contraceptive methods. Nevertheless, this factor does not influence women's contraceptive practice in 2017. Women of the endogenous (or traditional) religion were twice as likely not to use modern contraception as Christian women in 2017, while the risk was lower among women without religion (55.4%) in 2006. The results reveal that women in Alibori, Atacora, Borgou, Collines and Donga were less likely not to use contraception with a decrease in risk between 2006 and 2017. On the other hand, in 2017, women living in poorer households were less likely to use contraceptive methods compared to women from families with a very high standard of living, with 2.51 times the risk for the poorest and 2.04 times the risk for the wealthy economic class counterparts. It is also noted that in 2006, women who have had at least 4 children die have a high risk (10.26 times) of rejecting contraceptive methods. In 2017, this risk was estimated at 1.27 times for women who have lost only one (1) child compared to those who have never had a child die.

It is also noted that when the woman or the spouse/partner decides to use contraception alone, the probability of the woman using it within the couple were lower than if the decision was made by mutual agreement. This probability is estimated at 2.03 in 2006 and 2.12 in 2017 respectively. On the other hand, women whose husbands are undecided about their desire to have more children are 1.38 times more likely not to use modern contraceptive methods in 2006.Still, the effect of this variable was not significant in 2017.

Table 2: Relative risks of not using modern contraception among women in aunion between 2006 and 2017

Independent variable	EDSB-2006	EDSB-2017
	Model 1	Model 2
Exposure to mass media (Ref=Yes)		
No	0,859^{ns}	0,916^{ns}
Information on FP for community health workers (Ref=Yes)		
No	2,014***	0,996^{ns}
Religion (Ref=Christian)		
Endogenous	1,149^{ns}	2,052**
Muslim	1,015^{ns}	0,861^{ns}
Without religion	0,446**	1,290^{ns}
Place of residence (Ref=Urban)		
Rural	0,819^{ns}	1,027^{ns}
Department of residence (Ref=Coastal)		
Alibori	0,020***	0,364**
Atacora	0,098***	0,176***
Atlantic	1,884**	1,234^{ns}
Borgou	0,222***	0,131***
Hills	0,586*	0,147***
Couffo	0,354***	0,810^{ns}
Donga	0,328**	0,185**
Mono	0,436**	0,667^{ns}
Ouémé	0,839^{ns}	1,126^{ns}
Tray	0,188**	0,519^{ns}
Zou	1,094^{ns}	0,421**
Woman's level of education (Ref= Secondary and above)		
No	1,108^{ns}	0,804^{ns}
Primary	1,341^{ns}	0,860^{ns}
Age group (Ref=15-19yrs)		
20-29 years	1,310^{ns}	1,267^{ns}
30-39 years	1,478^{ns}	1,243^{ns}
40-49 years	0,922^{ns}	1,312^{ns}
Occupation of the woman (Ref=Administrative)		
Inactive	0,841^{ns}	0,746^{ns}
Farmer	1,380^{ns}	0,822^{ns}
Other sector	0,965^{ns}	0,871^{ns}
Household standard of living (Ref=Highest)		
poorer	1,035^{ns}	2,510**
Poor	1,277^{ns}	0,861^{ns}
Medium	1,300^{ns}	1,184^{ns}
Rich	1,027^{ns}	2,041***
Number of living children (Ref=0 child)		
1	0,861^{ns}	0,749^{ns}
2	0,747^{ns}	0,612^{ns}
3	0,615^{ns}	0,647^{ns}
4 or more	0,388^{ns}	0,315^{ns}
Number of children who died (Ref=0 child)		
1	1,273^{ns}	1,666**
2	1,049^{ns}	1,498^{ns}
3	2,075^{ns}	0,546^{ns}
4 or more	10,260**	3,385^{ns}
Contraceptive decision within the couple (Ref= joint decision)		
Woman	2,032***	1,135^{ns}

Independent variable	EDSB-2006	EDSB-2017
	Model 1	Model 2
Male	1,073^{ns}	2,118***
Spouse's desire for children (Ref=spousal desire for number of children)		
the husband wants more children	1,270^{ns}	0,967^{ns}
the husband wants fewer children	1,001^{ns}	0,557^{ns}
Don't know	1,384*	0,917^{ns}
Nickname R^2	0,154	0,129
chi2	222,540	116,637

Exponentiated coefficients ^{ns} $p < 1$,* $p < 0.10$,** $p < 0.05$,*** $p < 0.01$

3.4 Analysis of sources of change in contraceptive practices among women in union from 2006 to 2017

3.4.1 Analysis of differences due to characteristics

The result of the multivariate decomposition analysis showed that the composition effect accounts for 12.4% of the total difference in contraceptive prevalence. In other words, 12.4% of the difference in the proportion of women not using modern contraception is explained by differences in the characteristics of respondents between the 2006 and 2017 periods. In addition, the decrease in the proportion of women in union who do not use modern contraceptive methods is attributable to compositional factors such as: religion, department of residence, household standard of living, number of deceased children, and the person responsible for making decisions on contraceptive use within the couple. In addition, we note that a positive change in the behavior of women in union with regard to contraceptive methods residing in the departments of northern Benin (Alibori: 5.21%, Borgou: 2.52%, Atacora: 1.29%) has strongly contributed to the decrease in contraceptive prevalence among women who do not use modern methods. Women in the southern departments (Atlantique: 0.48977 and Zou: 0.54476) also contributed to this decline, but only slightly.

Similarly, women in endogenous religious unions (1.17%), women of wealthy economic class (0.64%) and women whose spouses adhere to contraceptive use (1.06%) contributed positively to the evolution of contraceptive practices between 2006 and 2017. Furthermore, although women from poorer households and those with one (01) child influence the upward trend in contraceptive practices, their effects are less noticeable with negative contributions of 1.29% (poorer) and 0.14% (1 child) respectively.

3.4.2 Analysis of differences due to coefficients

The analysis reveals that 87.5% of the total differences in contraceptive prevalence are due to coefficient differences. Of this, for an identical characteristic composition between the two periods, differences in the proportion of women not using modern contraceptive methods decreased by 35.82 percentage points. The coefficient difference reflects the effects associated with unobserved factors that could be the improvement over time of FP service offerings and reproductive behaviors of the population.

With regard to the observed variables, information on FP, religion, department of residence, standard of living and the couple's decision to use contraception are the factors significantly associated with the positive change observed in the use of modern contraceptive methods. Women in the department of Collines (8.70%) and those who take the lead in the couple (7.01%) in terms of contraceptive use have a preponderant share in the decline in the proportion of women not using FP over the periods 2006 and 2017. Women in a union who do not receive information on FP (9.97%) and who belong to poorer households (3.97%) show negative contributions to the observed percentage decline in non-users of modern contraceptive methods.

Table 3: Breakdown of the decline in contraceptive prevalence among women not using modern contraceptive methods in Benin from 2006 to 2017

Features	Effect of characteristics (E)		Effect of coefficients (C)	
	Coefficient	Share (%)	Coefficient	Share (%)
Aggregate effects	-0,050221	12,4	-0,35382	87,5
Constant			-0,25534	63,198
Information on FP for community health workers (Ref=Yes)				
No	7,7336E-05	0,019141	0,040272**	-9,9673
Religion (Ref=Christian)				
Endogenous	-0,0047382**	1,1727	0,012256	-3,0335
Muslim	-0,003239	0,80165	-0,0043047	1,0654
Without religion	0,00069595	-0,17225	0,0077251*	-1,912
Department (Ref=Coastal)				
Alibori	-0,021063**	5,2132	0,0092831**	-2,2976
Atacora	-0,0052091***	1,2892	0,0034626	-0,857
Atlantic	-0,0019789	0,48977	-0,01662	4,1136
Borgou	-0,010164***	2,5156	-0,0066568	1,6476
Hills	0,0091662***	-2,2686	-0,035148**	8,6992
Couffo	0,00040829	-0,101 05	0,0067433	-1,669
Donga	-0,0000018788**	0,000465	-0,0034446	0,85254
Mono	-0,0019886	0,49218	0,0030201	-0,74747
Ouémé	-0,001716	0,42471	0,0093718	-2,3195
Tray	-0,0025104	0,62134	0,0016197	-0,40087
Zou	-0,0022011**	0,54476	-0,015247*	3,7736
Household standard of living (Ref=Highest)				
poorer	0,0052311**	-1,2947	0,016045*	-3,9712
Poor	-0,00098084	0,24276	-0,0089547	2,2163
Medium	0,00036702	-0,09083 8	-0,0030457	0,75381
Rich	-0,0025917**	0,64146	0,030238**	-7,4838
Number of children who died (Ref=0 child)				
1 child	0,00056687**	-0,1403	0,010062	-2,4905
2 children	-0,00087913	0,21758	0,0049978	-1,237 ;
3 children	0,00025217	-0,062411	-0,0056867	1,4075
>= 4children	-8,7023E-05	0,021538	-0,0015746	0,38971
Contraceptive decision within the couple (Ref=joint decision)				
Woman	0,0038849	-0,96151	-0,028337**	7,0135
Male	-0,0042858**	1,0607	0,020996*	-5,1966

Exponentiated coefficients ^{ns} $p < 1$, * $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$

IV. DISCUSSIONS

From 2006 to 2017, at least 85% of women in union in Benin are not using modern contraceptive methods. The results show that this high prevalence of non-use of contraception is explained both by reasons given by non-users and by a number of socio-demographic, cultural and economic factors related to households.

Fear of side effects of contraceptive products and opposition from women are the real reasons for the rejection of modern contraception among women in a union from 2006 to 2017. The fear of health risks associated with the adoption of modern methods could be explained by the multiplicity of information sources, preconceived ideas, rumors or unfortunate experiences of some women. Studies have found similar results.

Bakyono R. and al (2020) found that the reluctance of married or cohabiting rural women in Burkina Faso was related to preconceived ideas and the resulting side effects. In Dibindi, DRC, although women are aware of modern

contraceptive methods, they refuse to use them because of the side effects (Ntambue A.M and al, 2017). However, the study by Rakotoarizay A.J.R. (2004), proves that contraceptive products produce side effects but not systematically in all women.

Religious discourses and practices influence both women's behavior and their attitudes towards contraception. The present study, like those of Smaïla O. and al (2022) in Burkina Faso and Iqramul H. and al (2017) in Bangladesh, found a significant association between religion and contraceptive use. Indeed, our work shows that in 2017, women in unions of endogenous religion are less likely to use modern contraceptive methods compared to Christian women. This result demonstrates the weight of culture in Beninese society as in most African countries. Furthermore, despite the influence of Western cultures, traditionalists remain supportive of trends that encourage increased reproduction. Consequently, they spread messages that discourage the use of all modern methods that can regulate birth. This may justify the rejection of modern contraceptives by some women.

Region of residence was found to be significantly associated with non-use of modern contraceptive methods in 2006 and 2017, respectively. Compared to women in the Littoral, most women residing in the other departments are less likely not to use contraceptives. This result is due to the various actions carried out by all development actors in the area of FP over many years, especially in the regions of northern Benin, which are known for their high fertility and very low contraceptive use. This favorable response is also due to the community development efforts noted throughout the country in recent years aimed at improving the well-being of the population.

Among others, women from higher social classes are more likely to use contraceptives than those from poorer categories (Igbodekwe F.C. and al, 2014). The same trend is evident in this study.

Thus, the likelihood of non-use of contraception is higher in the economically poorer category of women. Nduku and Simon-kengne (2022) came to the same results showing that poor Zambian women are more likely to not use any contraceptive method. These results indicate that the improvement in household economic well-being and women's status has not changed in a way that can significantly and sustainably influence women's contraceptive behavior.

In this study, the number of living children does not influence the non-adoption of modern contraceptive methods among married or cohabiting women. On the other hand, non-use of contraceptives is related to the number of deaths of children registered by the couple. It is believed that the concern to replace non-living offspring leads couples to opt for high fertility by rejecting all forms of contraception. This is what emerges from the work of Mwanza N V. and al. (2022) in the DRC, where the risk of not using contraception increases among women with fewer than four living children. Similarly Palamuleni M. (2013) in Malawi showed that contraceptive use increases with the number of children couples have alive.

In addition, joint decision making between partners to use contraception is a key determinant of contraceptive use among women in union during the period 2006-2017. A similar result is found in the work of Yina H. and al. (2022) among women of reproductive age in Mbeya, Tanzania.

These researchers showed that most women who had discussed family planning issues with their husbands or partners were in favor of contraceptive use, in contrast to women who had never discussed these topics with their spouses. It is therefore clear that the involvement of men in FP policies and programmes is necessary for their success and therefore actions should be taken to encourage couples to discuss FP more.

Thus, the husband's desire to have an additional child and lack of information about FP are risk factors for non-use of modern contraception in 2006. Tiruneh F. N. and al. (2016) had established a negative relationship between husbands' (spouses') desire for children and modern contraceptive use among Ethiopian

women in union. Asratie M.H. and al (2022) also found that the likelihood of non-use of contraceptives increases when husbands want more children or are unaware of their desire for children while the likelihood is lower among Ethiopian women in union who have received information about FP.

This highlights, on the one hand, the importance and social representation of the child in African society as mentioned in the literature review and the need to provide the couple in general with information on FP for behavioral change to improve their sexual and reproductive health on the other hand.

V. CONCLUSIONS

This study found that over the period 2006-2017, there is a downward trend in the proportion of married or cohabiting women who are not using modern contraceptives. This decrease of 6.3% is attributable to changes in characteristics and coefficients. In this regard, women in a union who have received information on FP, of endogenous religion or no religion, residing in the northern departments, economically poorer or richer, having a deceased child and whose decision to use contraceptives within the couple emanates from the woman or her partner are groups that have contributed overall to the positive evolution observed in the use of modern contraceptive methods between 2006 and 2017. On the other hand, despite this modest progress, the proportion of women who do not adopt modern contraceptives is still high. Fear of side effects and opposition from wives or husbands are the main reasons cited by women who refuse contraceptive methods. Among others, information on FP, religion, department of residence, household standard of living, number of deceased children, contraceptive decision and husband's desire to have children are the main factors of resistance to contraceptive use among married or cohabiting women in 2006 and 2017 respectively.

In light of these results, three actions can be taken. First, it is strongly recommended that development actors and the public authorities strengthen the various components of FP programmes throughout the country. Secondly, it is necessary to develop information and communication strategies directed mainly towards religious elites and disadvantaged populations for a positive change in behavior related to contraception and fertility. Finally, policies aimed at promoting reproductive health and the socio-economic conditions of women should be improved.

Conflict of Interest Statement

The authors state that there is no conflict of interest.

Ethical Approval

The data used for the estimates do not include confidential information about individuals or animals that may raise ethical concerns.

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Consent for Publication

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Data Availability Statement

The data used in this paper is fully available and can be accessed upon request.

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Takayasu Arteritis in Pregnancy: A Rare Case Report

Iata Assudani

ABSTRACT

Takayasu arteritis is a rare type of vasculitis, a group of disorder that causes large vessel inflammation. The disease can lead to narrowed or blocked arteries, or to aneurysm and tear. It may lead to complications like high blood pressure, heart failure, stroke, transient ischeamic attack and aneurysm in aorta. A healthy pregnancy is possible with the disease but it is a medical challenge. It usually complicates the latter half of the pregnancy and causes hypertension, organ dysfunction and feotal growth restriction. Pregnancy with TA is a medical challenge as the results of American college of rheumatology highlights the serious concerns ie miscarriage rate of 11% and intrauterine death of 1%, preterm delivery rate was 15%, 16% of pregnancies had IUGR and 28% of patients required delivery by LSCS (ACR). Here presenting a case of G4P3IUFD3 with previous 1 LSCS with Takayasu arteritis with chronic hypertension with late onset severe IUGR. Following a multidisciplinary approach, she delivered a live born female child with low birth weight. Her postpartum course remained uneventful. Despite advancements in cardiovascular management and new drugs, the optimal management for pregnant patients with this disease remains elusive.

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Takayasu Arteritis in Pregnancy: A Rare Case Report

lata Assudani

ABSTRACT

Takayasu arteritis is a rare type of vasculitis, a group of disorder that causes large vessel inflammation. The disease can lead to narrowed or blocked arteries, or to aneurysm and tear. It may lead to complications like high blood pressure, heart failure, stroke, transient ischeamic attack and aneurysm in aorta. A healthy pregnancy is possible with the disease but it is a medical challenge. It usually complicates the latter half of the pregnancy and causes hypertension, organ dysfunction and feotal growth restriction. Pregnancy with TA is a medical challenge as the results of American college of rheumatology highlights the serious concerns ie miscarriage rate of 11% and intrauterine death of 1%, preterm delivery rate was 15%, 16% of pregnancies had IUGR and 28% of patients required delivery by LSCS (ACR).

Here presenting a case of G4P3IUFD3 with previous 1 LSCS with Takayasu arteritis with chronic hypertension with late onset severe IUGR. Following a multidisciplinary approach, she delivered a live born female child with low birth weight. Her postpartum course remained uneventful. Despite advancements in cardiovascular management and new drugs, the optimal management for pregnant patients with this disease remains elusive.

I. INTRODUCTION

Takayasu arteritis (TA), also known as "young female arteritis", is a rare and chronic inflammatory disease of large vessels. The disease mainly affects women of reproductive age and Asian origin[1]. Moreover, TA leads to several complications including occlusion as well as aneurysm formation in systemic and pulmonary arteries. Its incidence is reported to be 13 cases per million population[2]. Pregnancy as such has no effect on the evolution of the disease, however, its peak incidence is in second and third trimesters.

Thus, such patients warrant special attention during peripartum period owing to likelihood of development of complications such as hypertension, multiple organ dysfunction and stenosis hindering regional flow leading to restricted intrauterine fetal growth and low birth weight in babies [3-5]. Delay in diagnosis is quite common, so patients often conceive without prior knowledge of having TA or having initiated specific treatment against it [6] Ideal management for pregnant patients with this disease still poses a stringent challenge, an interdisciplinary collaboration of obstretricians, cardiologists, rheumatologists and neurologists is often necessitated for an optimal maternal and fetal prognosis. Here is the case described to enlighten the obstretricians on fetomaternal outcome and management of this infrequent but not uncommon clinical entity encountered nowdays.

II. CASE HISTORY

A 28 years old female married since 7 years, spontaneous conception with 3 months of gestational age with known case of chronic hypertension non-compliant to medications was referred in view of renal artery color doppler suggestive of bilateral renal artery stenosis at origin. Atherosclerotic changes in the form of intimal thickening and calcification in the intima noted in the abdominal aorta and proximal superior mesenteric artery with surrounding tissue edema ? Aortoarteritis.

On examination, general condition of the patient was fair with pulse rate of 74/minute, BP being 160/100mmof hg in the left arm and 140/90mm of hg in right arm with negative urine albumin and pre-monitory signs and symptoms with

normal DTR, Spo2 99% on RA, absent pallor/ icterus/ edema.

Findings of CVS and RS were within normal limits

On P/A examination: soft, No GTR scar of previous LSCS+

P/S: cervix vagina healthy

P/V: uterus 12 weeks

B/L fornix free, non tender

She was admitted for further evaluation and management.

On admission, all routine investigations were within normal limits.

USG Obs+A+P was done S/O SLIUG of 12 weeks 2 days with hemodynamically significant bilateral renal artery stenosis.

CRP was negative, urine albumin negative, ESR 32

Nephrology reference was done, advised Quantitative ESR and CRP, APWA, VDRL, MR angiography of renal vessels and aorta with contrast.

Doppler study of B/L upper limb S/O no significant abnormality

USG KUB with renal doppler S/O hemodynamically significant B/L renal artery stenosis (right>left)

Carotid artery doppler unremarkable

MR Angiography S/O bilateral renal artery stenosis at the ostia, wall thickening and luminal irregularity involving the abdominal aorta, pseudoaneurysm formation in the abdominal aorta in the left side involving the suprarenal portion, nil flow detectable. Signal involving the superior mesenteric artery, the image S/O large vessel vasculitis (involving abdominal aorta, it's major branches and bilateral renal ostia) likely suggesting Takayasu arteritis.

2D echo S/O normal study with left ventricular ejection fraction 60%

Fundoscopy was done: Within Normal limits

USG obs NT scan done was S/O SLIUG of 13 weeks and 4 days.

Patient started on tab lobet 200mg TDS and tab aspirin 75mg OD with twice daily BP charting at home.

Patient was following up regularly for ANC visits and was admitted again in view of raised BP not controlling on antihypertensives at 26 weeks of gestation.

BP monitoring done and antihypertensives adjusted accordingly, started on tab nicardia 30XL QID and tab lobet 400-200-400 and tab prednisolone 20 mg OD to reduce disease progress.

Repeat rheumatology refernce done, advised to control BP aggressively. She should not go into preeclampsia and eclampsia, further treatment after delivery as patient will require stenting.

Patient was taken for emergency LSCS at 31 weeks of gestation in view of USG S/O uteroplacental and fetoplacental insufficiency with prev LSCS with short ICP after confirmation of NICU bed and ventilator.

Baby cried immediately after birth and was admitted in NICU in view of Extremely preterm and very low birth weight of 1.1kg.

Patient was shifted to CCU for post-operative monitoring which was uneventful. Interventional radiologist reference done in view of definitive management of Takayasu arteritis and was advised PET CT and stenting after funds are available.

Patient was discharged with baby on day 36 PNC.

III. DISCUSSION

Takayasu arteritis was first described in 1908 by 2 Japanese opthalmologists, Mikito Takayasu and onishi, who observed retinopathy in the absence of peripheral pulses. The cause is unknown, but it seems to be related to autoimmunity, sex hormone (more common in young females) and genetics (demonstrated by the predisposition of the human leukocyte antigen-HLABW52).

Disease progression typically occurs in various stages from acute inflammatory arteritis to lymphocytic infiltration, intimal thickening, elastic tissue destruction, fibrosis and patchy minimal narrowing of arteries.

Depends on angiographic classification there are five types based on the involvement arteries [1,7] .

Type I involves branches of aorta

Type IIa involves ascending aortoaortic arch and its branches.

Type IIb involves type IIa and thoracic descending aorta.

Type III involves thoracic descending aorta, abdominal aorta, renal arteries or combination.

Type IV involves abdominal aorta, renal arteries or both.

Type V involves entire aorta and its branches. Stage 1 (prevasculitic systemic stage) constitutional symptoms like fatigue, malaise, giddiness, fever

Stage 2 (vascular inflammatory stage) -stenosis, aneurysms and vascular pain(carotidynia)

Stage 3 (burned-out stage)-fibrosis and generally associated with remission.

The incidence of Takayasu arteritis during childbearing years is relatively high, the management of pregnancies with this disease is of great importance in clinical obstetrics. Pregnancy with Takayasu arteritis can be complicated by hypertension, as seen in our case, and worsening of cardiovascular hemodynamic status. Hypertension is a serious complication that can lead to intrauterine growth retardation, fetal hemorrhage, and maternal heart failure [8] . The increased intravascular volume seen during pregnancy may impair circulation and exacerbate maternal hypertension, aortic regurgitation, and congestive heart failure [9].

The disease causes various clinical conditions depending on the sites of constriction such as arm claudication, decreased arterial pulses, visual loss, stroke, aortic regurgitation, Hypertension, congestive cardiac failure. Hypertension is seen in 90% cases Takaysu arteritis. The clinical patterns of TA differ at the acute and chronic periods. In the acute period, systemic symptoms prevail, while in the chronic period, insidious ischemic-destructive signs are more prevalent.

These signs appear together with stenosis at a rate of 85%, dilatation at a rate of 2%, and stenosis and dilatation at a rate of 13% [10,11,12].

The symptoms range from fever, fatigue, and weight loss to life-threatening hemoptysis and heart failure.

Diagnosis is usually based on clinical manifestations, inflammatory markers (acute phase reactants), and arteriography demonstrating aortic stenosis and of its branches.

Common features of active TA are fatigue, myalgia, arthralgia, and low-grade fever in initial stages and intermittent claudication, visual defects, and fainting attacks in later stages. Many may be diagnosed after clinical examination, when one or more peripheral pulses are not palpable or blood pressures vary in two limbs.

However, computed tomography or magnetic resonance angiography can detect TA even before the development of severe vascular compromise as in our case [13]

B Recently, 18 FDG-PET scan has been added as an adjunct imaging modality in the armamentarium of rheumatologists and cardiologists to diagnose LVV, with a pooled sensitivity and specificity of 70.1% and 77.2%, respectively[14]. But this is currently not available in our hospital.

However, the gold standard for diagnosis still remains as vessel biopsy [10] which could not be performed in our case.

The management of TA is a multidisciplinary approach with the involvement of obstetricians, anesthesiologists, cardiologists, rheumatologists, and neonatologists. Ultimately, the aims encompass the control of inflammation, prevention, and treatment of complications like hypertension and occlusive or stenotic lesions [15]. The aims are control of inflammation, prevention and treatment of complications like hypertension and revascularization by percutaneous angioplasty, use of endoprosthesis, or surgical correction for occlusive and stenotic lesions.

When managing women of reproductive age with TA, preconception counseling is essential. In addition, such counseling will focus mainly on dosage adjustment, cessation of cytotoxic drugs, folic acid supplementation in the

periconception period, and the optimal timing of pregnancy. Similarly, the pregnancy should be ideally planned in remission phase and patients are encouraged to pursue an early booking for regular antenatal supervision. In addition to routine antenatal visits, serial monitoring of BP, renal function, cardiac status, and pre-eclamptic screening is vital in such patients. Furthermore, fetal surveillance is also necessary and will include daily fetal kick count, gravidogram, serial fetal biometry, biophysical profile, and fetal Doppler [16]

Controlling BP during pregnancy may be difficult due to the physiological changes in this period.

Thus, any patient with TA should plan to conceive when the BP and disease are stable. It is also vital to adjust the antihypertensive medication and avoid angiotensin-converting enzyme inhibitors or angiotensin inhibitors. On the other hand, uncontrolled hypertension during pregnancy has been associated with abortion, stillbirths, aortic dissection, cardiac and renal insufficiency, stroke, and maternal death [17-19].

Antihypertensive drugs and antiplatelets can be started as per need, as was in the present case. TA may respond symptomatically to corticosteroid therapy (first line drugs) at a dose of 1-2 mg/kg/bodyweight for 4 weeks followed by slow tapering. However, chronic use of corticosteroids could lead to suppression of adrenal gland activity with inadequate release of endogenous corticosteroids in moments of stress, such as surgeries [20]. Also immune-suppressors including methotrexate and azathioprine are used.

Finally, vaginal delivery has proven to be the preferred mode of labor management for patients with TA. Additionally, epidural analgesia has been advocated for labor and delivery as well and delivery abbreviated by use of forceps. In our case, decision for emergency LSCS taken in view of USG S/O uteroplacental and fetoplacental insufficiency with previous lscs with short ICP and was uneventful.

Patient was monitored postoperatively in CCU and was transferred to medicine for further management, where patient continued on steroids as she was breast feeding and methotrexate was contraindicated and discharged with advise to monitor BP and follow up with BP charting after 3 months for revasvularisation surgery.

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Adrenal Myelolipoma: A Rare Case of the Incidentaloma: About One Case

Iken Taha

ABSTRACT

Background: Adrenal myelolipoma is a rare, benign, non-functioning tumor of the adrenal gland. Which is why it is often asymptomatic, but it may be complicated by pain or retroperitoneal hemorrhage. Medical imaging is key to the diagnosis by highlighting its fatty component, non present in other adrenal incidentalomas. Surgery is indicated when there is a large or Complicated Myelolipoma. We report the case of a large symptomatic adrenal myelolipoma discovered in a 50 year old woman.

Case report: We describe a case of an 8cm non-functional, and heterogenous right adrenal myelolipoma discovered on a routine computed tomography (CT) scan evaluation for cervical cancer in a 50 years old woman.

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Case report: We describe a case of an 8cm non-functional, and heterogenous right adrenal myelolipoma discovered on a routine computed tomography (CT) scan evaluation for cervical cancer in a 50 years old woman.

I. INTRODUCTION

Adrenal myelolipoma is a rare, benign, non-functioning tumor of the adrenal gland. Which is often asymptomatic, but it may be complicated by pain or retroperitoneal hemorrhage. Medical imaging is key to the diagnosis by highlighting its fatty component, non present in adrenal incidentalomas. Surgery is indicated when there is a large or Complicated Myelolipoma. We report the case of a large symptomatic adrenal myelolipoma discovered in a 50 year old woman.

II. OBSERVATION

The patient was a 50 year-old married woman, G8P5, diabetic, with a history of cervical cancer, was referred to our institution for an adrenal mass found on a Ct scan performed to assess her cervical cancer. Ct scan revealed a well-defined 8 cm Heterogenous mass of the right adrenal gland. The patient exhibited no clinical signs of adrenal dysfunction : the clinical evaluation was normal.

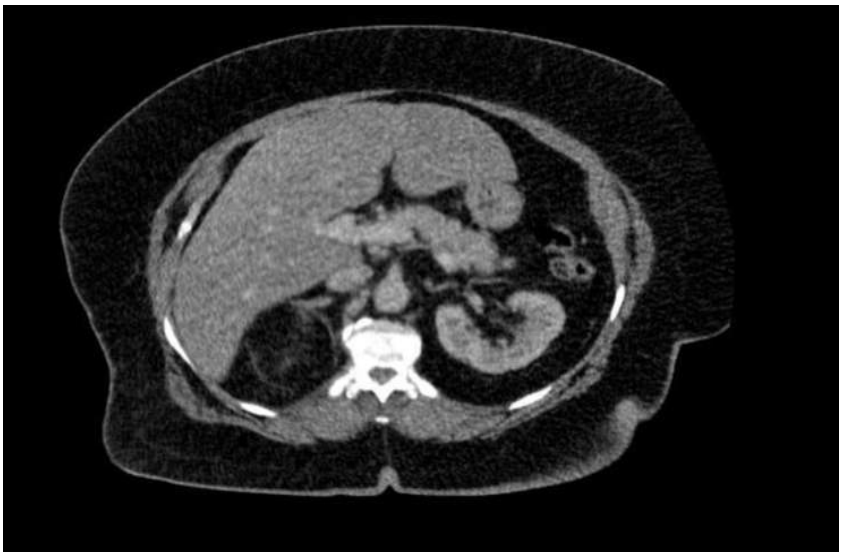

Figure 1: Axial C+ abdominal stage in portal phase showing a right adrenal mass with sharp and regular contours, hypodense (- 110 HU) not enhancing after contrast injection

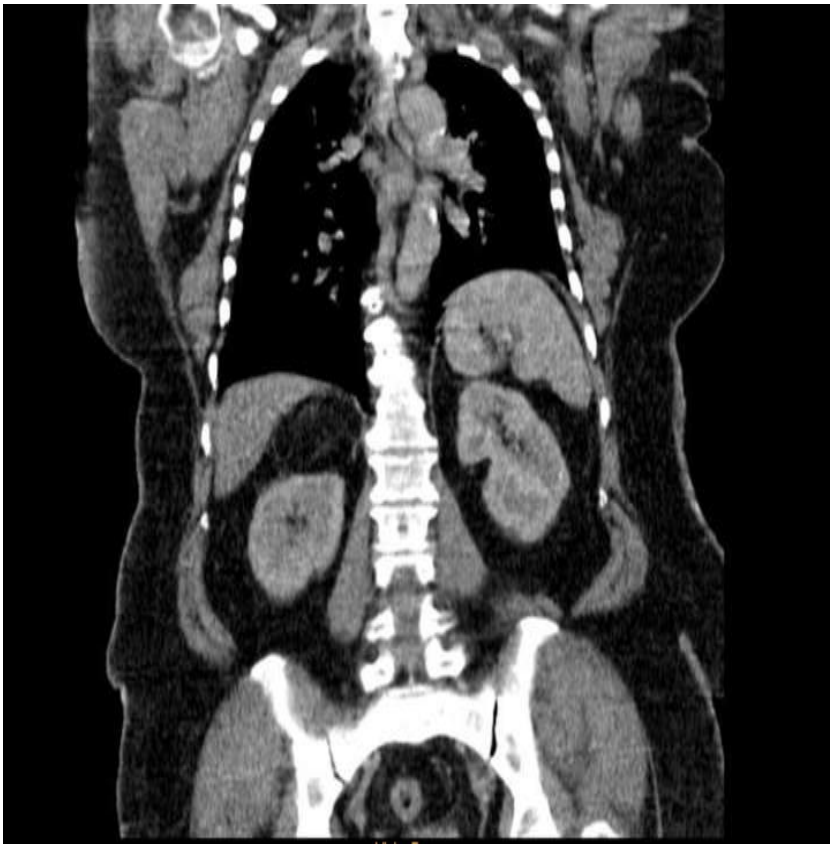

Figure 2: Coronal C+ abdominal stage in portal phase showing a right adrenal mass with sharp and regular contours, hypodense (- 110 HU) not enhancing after contrast injection

Figure 3: Sagittal C+ abdominal stage in portal phase showing a right adrenal mass with sharp and regular contours, hypodense (- 110 HU) not enhancing after contrast injection

III. DISCUSSION

Once considered an autopsy curiosity, adrenal myelolipoma is now increasingly diagnosed with the frequent use of modern imaging methods. In a recent meta-analysis, fewer than 100 cases were reported(1). The real incidence of adrenal myelolipoma is difficult to determine because of its rarity and its mostly asymptomatic character(2). It is estimated to be between 0.08 and 0.2% in old autopsy series(3).

It is most often discovered in the fifth decade of life (extremes from 17 to 93 years) with a slight male predominance. Adrenal myelolipoma is most often unilateral, and is frequently associated with obesity, high blood pressure (HTA), endocrine disorders or various tumor diseases (3) (4).

The origin of these tumors remains poorly understood. The metaplastic theory is the most widely accepted: the adrenal myelolipoma would derive from reticular cells of the adrenal cortical framework in response to an infection, to necrotic lesions of the adrenal gland or to chronic stress (4).

Adrenal myelolipoma is a non-secreting tumor that does not cause any adrenal hormonal dysfunction. It is most often asymptomatic(5).

It may manifest itself by non-specific symptoms consisting of nonspecific abdominal pain secondary to the mass effect in the case of large tumors, or intratumoral hemorrhagic and necrotic phenomena 2'. high blood pressure may be observed in case of compression of a renal artery.

Rarely, due to tumor rupture, patients may present with acute back pain, associated with a state of hypovolemic shock secondary to retroperitoneal hemorrhage. This is a serious complication that can be life-threatening and require emergency surgery (6).

Imaging studies are most often helpful in making the diagnosis and differentiating adrenal myelolipoma from other adrenal incidentalomas by demonstrating its fatty component 2".

Ultrasound typically shows a markedly hyperechoic adrenal mass of solid nature. CT scan is the gold standard for the diagnosis. It usually shows a well-limited adrenal formation, which may be septate or contain fine calcifications that displace the healthy adrenal parenchyma. It allows above all to detect the fatty contingent of the tumor characterized by a negative density of -50 to -100 UH (7).

Sometimes, the diagnosis can be more challenging when there are some hemorrhagic changes or preponderance of the myeloid component masking the "fatty" character; the adrenal myelolipoma may then appear hypoechoic on ultrasound and hyperdense taking the contrast medium on CT. This appearance may be confused with a pheochromocytoma or a non-secreting adrenal carcinoma or even a renal angio-myolipoma. In these situations, magnetic resonance imaging (MRI) can be useful and allow a better tissue characterization of the components of the adrenal myelolipoma by demonstrating a clear hypersignal on T1-weighted sequences and a T2 signal attenuation for the fatty component as well as a hyposignal in T1 and an intermediate signal in T2 for the hematopoietic component.

In case of persistent diagnostic doubt, particularly in patients with a history of extrasensory neoplasia, or in bilateral forms, fine needle aspiration guided by ultrasound or ct scan with cytological study is justified and can sometimes avoid unnecessary surgery.

Adrenalectomy is the primary treatment and may be indicated in the following settings: painful forms, complicated forms (hemorrhage, compression), doubt on a malignant component. With the progress made in laparoscopic surgery, surgical excision is increasingly recommended by this route(8).

Management of asymptomatic adrenal myelolipoma, is controversial. They are most often simply monitored by imaging. However, any increase in volume during follow-up will warrant surgical removal, given the risk of haemorrhagic complications.

A few authors systematically indicate surgical removal from the outset, while others reserve this attitude for large tumors (8).

Regular monitoring, based mainly on CT, is necessary because of the possibility of development of lateral adrenal myelolipoma.

The prognosis after surgical treatment is good, with recurrence-free follow-ups of up to 12 years.

IV. CONCLUSION

Adrenal myelolipoma is a benign tumor, rare and often asymptomatic of incidental discovery.

Imaging usually allows the diagnosis to be evoked. The complicated, sympathetic or voluminous nature of the adrenal myelolipoma should indicate surgical removal with anatomopathological confirmation. otherwise, surveillance by imaging is recommended.

Autoimmune Responses and the Roles of Virus Infections, Complimentary Peptides, Phosphatidylserine and Physiologic Checkpoint Molecules in their Generation

James R Kennedy

ABSTRACT

When there are two complimentary peptides on the class I major histocompatibility (MHC) complexes present on a cell's surface and the foreign peptide present on a virus binds to a complimentary peptide on the class I MHC of one of them this will produce both an adaptive, and an innate autoimmune response. The adaptive response will be to the foreign virus peptide exposed on the class I MHCs of the infected cells and the innate autoimmune response will be to the self-peptide exposed on the uninfected cells that are complimentary to the peptide the virus binds to. The cytotoxic T cells (CTLs) generated in adaptive immune responses will have peptides on their T cell receptors (TCRs) that are complimentary to the foreign peptide exposed on the class I MHC of the infected cells and to the identical self-peptides on the class I MHCs of uninfected cells.

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James R Kennedy

ABSTRACT

When there are two complimentary peptides on the class I major histocompatibility (MHC) complexes present on a cell's surface and the foreign peptide present on a virus binds to a complimentary peptide on the class I MHC of one of them this will produce both an adaptive, and an innate autoimmune response. The adaptive response will be to the foreign virus peptide exposed on the class I MHCs of the infected cells and the innate autoimmune response will be to the self-peptide exposed on the uninfected cells that are complimentary to the peptide the virus binds to. The cytotoxic T cells (CTLs) generated in adaptive immune responses will have peptides on their T cell receptors (TCRs) that are complimentary to the foreign peptide exposed on the class I MHC of the infected cells and to the identical self-peptides on the class I MHCs of uninfected cells.

When there are two complimentary peptides on the class I major histocompatibility (MHC) complexes present on a cell's surface and the foreign peptide present on a virus binds to a complimentary peptide on the class I MHC of one of them and infects it this will produce both an adaptive immune response to those cells and complimentary peptides on the T cell receptors (TCRs) of the cytotoxic T cells (CTLs) generated there will bind to Stop 2/23/2023 to the, immune response to the and an innate autoimmune response.

The adaptive response will be to the foreign virus peptide exposed on the class I MHCs of the infected cells and the innate autoimmune response will be to the self-peptide exposed on the uninfected cells that are complimentary to the peptide the virus binds to. The cytotoxic T cells (CTLs) generated in adaptive immune responses will have peptides on their T cell receptors (TCRs) that are complimentary to the foreign peptide exposed on the class I MHC of the infected cells and to the identical self-peptides on the class I MHCs of uninfected cells.

Cells are damaged in all three immune responses resulting in phosphatidylserine (PS) on their surface where it.

I. INTRODUCTION

All biologic molecules are made of peptides and eukaryotic vertebrate cells expose their self-peptides on the class I major histocompatibility complexes (MHC) present on the surface of their membranes.

Viruses are protein molecules made by the eukaryotic cells of vertebrate species that apparently have no intracellular functions or extra cellular function such as proteins involved in blood coagulation and immune responses but if and when they gain access to the external surface of the epithelial pulmonary or gastrointestinal surface they may become infectious pathogens.

Viruses are protein molecules made by the eukaryotic cells of vertebrate species that apparently have no intracellular or extra cellular functions but if and when they gain access to the external surface of the epithelial pulmonary or gastrointestinal surface they may become infectious pathogens.

For a virus to infect eukaryotic cells a foreign peptide or peptides on its surface must first be

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complimentary to a self-peptide on the class I MHC and then if it's successful in gaining entrance into it its RNA or DNA directs its replication.

A foreign peptide is one that isn't exposed on a class I MHC molecule but is complimentary to one that is.

When the virus infected cell replicates and it gains access to plasma in blood vessels the foreign peptides on its surface bind complimentary self-peptides on the toll like receptors of macrophages, dendritic cells and B cells and they phagocytize, disassemble them and expose the foreign peptide on the class II MHC of the dendritic and B cells to initiate the adaptive immune response.

The hypotheses proposed here are that autoimmune immune responses are initiated by virus infections when the foreign peptides on them bind to one of two complimentary peptides on the MHCs of a cell, that the phosphatidylserine (PS) molecule is exposed on the TMEM16 Fscramblase molecule in both the innate and adaptive immune responses where it generates physiologic checkpoint molecules (CPMs) that influence the outcomes of all three immune responses.

In the following we will very briefly examine inflammation, blood coagulation, the innate and adaptive immune responses and the presumptive generation of physiologic checkpoint molecules (CPMs) generated in innate immune responses that influence the generation of the innate, adaptive and autoimmune responses.

Phosphatidylserine (PS) molecules are present on the membranes of all eukaryotic cells where they are kept on their cytoplasmic surface in an energy dependent manner but when the eukaryotic cells of vertebrates are physically damaged and when pathogens breach the vertebrate's epithelial barriers PS moves to their surface.

When the vertebrate cells are physically damaged the PS moves to their surface by the TMEM16 F scramblase molecule where it activates inflammation, activates all immune cells in an innate immune response by binding to their TIM and TAM receptors and it becomes the platform upon which the coagulation cascade generates thrombin.

When pathogens infect vertebrates the foreign peptides on the pathogens bind to self-peptides on the toll like receptors on immune cells and generate an adaptive immune response that generate foreign peptide specific cytotoxic T cells (CTLs) and antibodies.

When cells die by programed cell death (PCD) and when they are lethally damaged caspase molecules direct PS exposure by the Xkr8 scramblase molecule where PS binds to TIM receptors on macrophages by the PS bridging molecule MFC-E8 and activates the phagocytosis of the PS+ cells.

Except for the macrophages that phagocytize the billions of cells that die by programmed cell death (PCD) each day the myelocytic and lymphocytic immune cells are predominantly dormant but when eukaryotic vertebrate cells are physically damaged and when pathogens with foreign peptides on their surface breach the vertebrates epithelial barriers they are activated.

Foreign peptides are those on the surface of pathogens that *aren't exposed* on class I MHC molecules but *are* complimentary to self-peptides exposed on class I MHC of eukaryotic vertebrate cells.

PS is present on the membranes of all eukaryotic cells where it's kept on their cytoplasmic surface in an energy dependent manner but it moves to their surface by the TMEM16F scramblase molecule when they are physically stressed or damaged and by the Xkr8 scramblase molecule when they die by PCD.

When cells are physically damaged calcium enters them and PS is exposed on TMEM16 F where it generates inflammation, activates *all* immune cells in innate immune responses by binding to their TIM and TAM receptors and becomes the platform upon which the coagulation cascade generates thrombin in blood coagulation.

Caspases activate PS exposure by the Xkr8 scramblase molecule on cells dying by PCD where

the PS on their surface binds to the PS bridging molecules MFG-E8 and they bind to TIM receptors on macrophages and activate them to phagocytize, disassemble and recycle their peptides.

When the foreign peptide on a virus bind to one of two or more complimentary peptides on a cell the cytotoxic T cells (CTLs) generated in the adaptive responses will have peptides on their T cell receptors (TCRs) that are complimentary to the foreign peptides on the class I MHC of the infected cells and to uninfected cells in the autoimmune response.

When the adaptive response has eliminated the virus the peptides on the TCRs of the CTLs will continue killing uninfected cells with peptides on their class I MHC that were complimentary to the peptide on the that the vi.

When the CTLs with peptides on their TCRs that are complimentary to the peptides on one of two peptides surface of the cells they infect they will.

In the CTLs generated when a virus binds to the foreign peptide on the class I MHC of a cell that has a complimentary peptide on another of its class I MHC molecules the peptide on the CTLs TCR will he peptides on the TCR of the CTLs.

The kind of cell the foreign peptide binds determines the kind of autoimmune response generated against uninfected cells as is demonstrated when it binds to a beta cell that secretes insulin.

It is also proposed that physiologic checkpoint molecules (CPMs) are generated whenever PS is exposed on TMEM16F and in autoimmune responses the

The hypotheses proposed are that autoimmune immune responses are initiated by virus infections when the foreign peptides on them bind to one of two complimentary peptides on the MHCs of a cell, that the phosphatidylserine (PS) molecule is exposed on the TMEM16Fscramblase molecule in both the innate and adaptive immune responses where it generates physiologic checkpoint molecules (CPMs) that influence the outcomes of all three immune responses.

In the following we will very briefly examine inflammation, blood coagulation, the innate and adaptive immune responses and the presumptive generation of physiologic checkpoint molecules (CPMs) generated in innate immune responses that influence the generation of the innate, adaptive and autoimmune responses.

Inflammation

Inflammation begins in adaptive immune responses when foreign peptides on pathogens bind to complimentary peptides on the toll like receptors of macrophages and dendritic cells and activate their secretion of inflammatory cytokines that stress somatic cells and expose PS on their surface by TMEM16F.

Inflammation begins in innate immune responses when PS is exposed on physically damaged cells by TMEM16F and peptides on its surface bind to TIM receptors on macrophages and dendritic cells. In both immune responses inflammation is generated when PS binds to the TIM-1 receptor on CD4 Th1 immune cells and activates their feedback secretion of inflammatory cytokines that stress somatic cells and expose PS on their surface. This was documented in 2017 when mice were infected with the Ebola virus and PS exposed on its surface produced a lethal cytokine storm. When TIM-1 knockout mice were infected by Ebola the mice survived and an inflammatory cytokine storm didn't develop. In that experiment the viral load was only minimally reduced proving that the PS on the virus, not the virus itself produces the inflammation. Inflammation is a physiologic action that amplifies adaptive immune response to respond to rapid pathogen generation but the Ebola virus is a long linear enveloped virus with PS exposed all over its surface and in the septicemia generated in an Ebola infection the PS numbers produce pathology. The same thing happens in other infections when PS exposure is excessive and also in massive trauma.

Blood coagulation

Blood coagulation begins whenever cells are stressed or damaged and tissue factor (TF) and PS are exposed with the TF initiating blood coagulation and PS amplifying it by being the

platform upon which the coagulation cascade generates thrombin [5,8]. TF activates factors IX and X and activated factor Xa changes prothrombin to thrombin and the thrombin activates PS exposure on platelets and initiates the cascade's feedback thrombin generation. The TF activated factor IX is essential for cascade function and as such is a rate limiting component of blood coagulation. Thrombin generated by the cascade binds to factor XI and activates it to bind to factor IX to maintain cascade thrombin generation and for maximum thrombin generation activated factor XIIa will bind to factor XI and activate its factor IX activation. However factor XII can't be activated intravascularly because it must bind to sulfatide exposed on the surface of activated platelets and activated platelets secrete a factor XII activation inhibitor.

When vascular walls are breached collagen is exposed and PS+ activated platelets with sulfatide on their surface bind to it and the factor XII activation inhibitor is washed away and maximal thrombin generation takes place at the breach.

Immune cell activation and autoimmunity

In an autoimmune response initiated by a virus there will be an adaptive immune response to the foreign peptide exposed on the class I MHC of an infected cell and an innate response to self-peptides on the class I MHCs of a cell when CTLs generated in the adaptive response bind to identical peptides on the MHC of non-infected cells and damage and kill them.

Adaptive immune response

In an adaptive response the foreign peptides on the surface of a virus bind to self-peptides on the surface of toll like receptors on macrophages, dendritic cells and B cells and activate them to secrete inflammatory cytokines and to phagocytize, disassemble and expose their peptides on their MHC molecules.

The inflammatory cytokines stress somatic cells and they expose PS on their surface that binds to TIM-1 receptors on Th1 immune cells and they secrete more inflammatory cytokines to amplify the innate response.

The viral self-peptides are exposed on those cells class I MHC and its foreign peptides are exposed on the class II MHC of dendritic cells and B cells.

The foreign peptides on the class II MHC of the dendritic cells bind to complimentary self-peptides on the class I MHC of CD4 and CD8 T cells and activate them.

The self-peptides on the activated CD4 cells bind to foreign peptides on the class II MHC of B cells and they secrete foreign peptide specific antibodies that cloak viruses generated by infected cell to prevent more cells from being infected.

They will also bind to pathogens and be joined there by compliment that enables their removal.

The activated cytotoxic CD8 T cells (CTLs) will have peptides on their T cell receptors that are complimentary to the foreign peptides on class I MHC of infected cells and kill them.

Innate immune responses

Innate immune responses repair physically damaged tissues and those innate responses are activated when PS is exposed by TMEM16F and it binds to complimentary peptides on the TIM and TAM receptors that are both present on the surface of each immune cell and they are activated to secrete cytokines that direct the repair.

Peptides on PS aren't complimentary to TAM receptors and must bind to complimentary peptides on the Gas6 and ProS bridging molecules and peptides on them bind to peptides on the Tyro3, AXL and Mer TAM receptors.

It proposed that TIM and TAM receptors are on/off switches that are activated by *some* PS peptides binding directly to TIM receptors on all immune cells and secreting cytokines to turn them on and *other* PS peptides binding indirectly to TAM receptors to secrete turn them off.

Other PS

It is also proposed the that individual peptides on PS bridging molecules determine which immune cells need to be turned off in innate immune

responses but that they all secrete the same off cytokine switch.

That cytokine switch has a peptide on it that is complimentary to the PS receptors on activated CTLs and macrophages and prevents them from recognizing and killing and phagocytizing physically damaged cells in innate immune responses.

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